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RESEARCH PAPER

Preparation and Evaluation of New Cellulose Acetylsalicylate Chiral Stationary Phase

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Abstract: Cellulose acetylsalicylate chiral stationary phase (ACSP) was synthesized by using cellulose and *o*-acetylsalicylryl chloride, and its enantioseparation ability was evaluated by high performance liquid chromatography (HPLC). Commercial Chiralcel OJ column was evaluated for comparison. The effects of mobile phase composition and double ester carbonyls of derivative on enantioseparation were investigated. The structure of the obtained derivative was characterized by infrared (IR) spectroscopy and thermogravimetric analysis. Hexane-isopropanol (90:10–80:20, *V/V*, 0.1% DEA or TFA) was selected by comparison of four mobile phases, namely hexane-isopropanol, hexane-ethanol, hexane-methanol-isopropanol and hexane-methanol-dichloroethane. Seven racemates of catecholamines and amides were used to evaluate its chiral recognition ability in normal phase elution mode, and the regularity and characteristics of the novel chiral stationary phase were explored. The chromatographic results showed that cellulose ACSP exhibited high enantioseparation ability for catecholamines and some racemates with amide group due to the hydrogen-bond, dipole interaction of carbonyls of acetylsalicylate and the π-π interaction with benzene ring, and the optimum amount of diethylamine or trifluoroacetic acid was 0.1%.

Key Words: Acetylsalicylate; Cellulose; Chiral stationary phase

1 Introduction

It is well known that enantiomers of a given compound may possess completely different physiological and biological activities, and diverse pharmacodynamic and pharmacokinetic characteristics [1,2]. Isolation of optical isomers is hence a central issue especially at the early stage in drug discovery process. The development of efficient and rapid enantioseparation and determination methods for chiral drugs is of great importance in the clinical applications[3,4].

Statistically, more than 90% of enantiomeric samples can be enantioseparated by chiral liquid chromatography (LC) using cellulose derivatives-based chiral stationary phases (CSPs)[5–7]. The chiral recognition abilities of the cellulose benzoate derivatives depend on the substituents on the phenyl groups[8,9]. These substituents seem to influence the polarity of the benzoate group through an inductive effect, thus further influence the interaction mode between the cellulose derivatives and the chiral compounds. On the other hand, the chiral recognition ability of the phenylcarbamate derivatives is also influenced by the position of the substituents on the phenyl group of the polymer. These substituents are all simple alkyls or halogen so far. However, cellulose is a polyhydroxylated compound and there should be many kinds of cellulose derivatives in theory. Based on these facts, acetylsalicylryl chloride is believed to be a potential derivatization reagent of cellulose for chiral separation. Its cellulose derivative has two ester groups (electron-donating) in positions 1 and 2 of the phenyl moiety of the polymer. Until now, no application of this derivative in researches of chiral separation or cellulose has been reported. In this work, cellulose acetylsalicylate chiral stationary phase (ACSP) was

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prepared and the chiral recognition ability towards the enantiomers of 7 analytes was evaluated and compared with that of Chiralcel OJ. The experiment results of this work may provide new strategy for development of new cellulose derivatives for enantioseparation.

2 Experimental

2.1 Apparatus and materials

Nicolet370 FT-IR spectrometer (Thermo, USA) and Q500 thermogravimetric analyzer (Waters, USA) were used for the structural characterization and analysis. LC-30A high performance liquid chromatography work station (Shimadzu, Japan) equipped with SPD-M20A photo-diode array detection system. Chiralcel OJ column was provided by Henan Provincial Institute of Food and Drug Control, China.

Microcrystalline cellulose (DP ≈ 100) was from Merck, Germany. Acetyl salicylic chloride and 3-aminopropyltrieth-oxysilane (KH-550) were purchased from Aladdin Chemicals (Shanghai, China). HPLC-grade spherical silica gel (particle size of 5μm, pore size of 120 Å) was obtained from Daiso (Japan). HPLC-grade solvents were purchased from Merck (Germany). Dimethylacetamide (DMAc), LiCl and pyridine were purchased from Tianjin Kemiou Chemical Reagent Co. (China). Seven chiral analytes were obtained from National Institutes for Food and Drug Control, China, and the structures are shown in Fig.1.

2.2 Synthesis of esterified cellulose derivative

After vacuum drying at 80 ºC for 6 h, 1.0 g of cellulose was added in 40 mL of absolute DMAc, and then subjected to refluxing under constant stirring at 130 ºC for 2 h. After cooling down to room temperature, 3.0 g of anhydrous LiCl was added into the reaction mixture. After a homogenous and transparent cellulose solution was obtained[10] under stirring, the reaction mixture was heated to 100 ºC, followed by the addition of 7.4 g of acetyl salicylic chloride and 8 mL of pyridine. Then the mixture was allowed to react at 100 ºC for 24 h. The product was precipitated and washed by excess methanol, and then filtrated. After vacuum drying at 40 ºC overnight, 5.6 g of esterified cellulose derivative was obtained. The synthesis process is depicted in Fig.2.

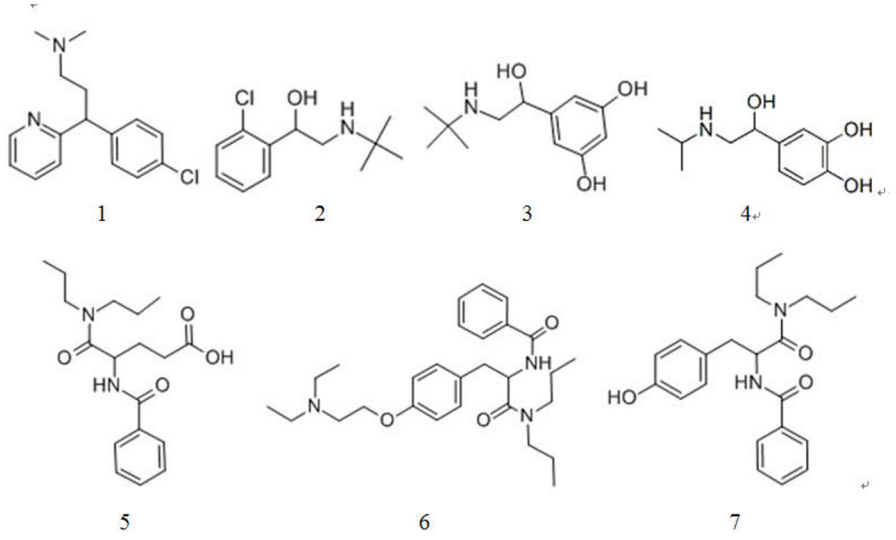

Fig.1 Structures of racemates (1–7)

1. Chlonpheniramine; 2.Tulobuterol; 3. Terbutaline; 4. Isoproterenol; 5. Proglumide; 6. Tiropramide; 7. *N*-Benzoyl-*DL*-tyrosil-*N*′,*N*′-dipropylamide

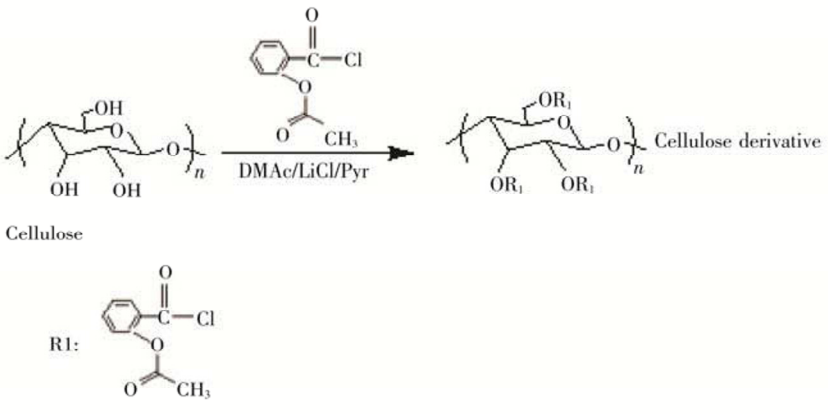

Fig.2 Synthesis of cellulose derivative